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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT	PAPER NUMBER
	6

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐

Part II SUMMARY OF ACTION

1. ☒ Claims 1-28 are pending in the application.
   Of the above, claims 5-11, 14-28 are withdrawn from consideration.
2. ☐ Claims have been cancelled.
3. ☐ Claims are allowed.
4. ☒ Claims 1-4, 12, 13 are rejected.
5. ☐ Claims are objected to.
6. ☒ Claims 1-28 were subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on [illegible]. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on [illegible], has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-4,12-23, drawn to DNA, vectors, cells and a process of making the LERK-6 polypeptide, classified in classes 435 and 536, subclasses 69.5 and 23.5 respectively.

II. Claims 5-11, drawn to LERK-6 polypeptides, classified in class 530, subclass 351.

III. Claims 24-25, drawn to antibodies, classified in class 530, subclass 389.2.

IV. Claim 27, drawn to transgenic mammal, classified in class 800, subclass 2.

V. Claim 28, drawn to a method of separating cells, classified in class 435, subclass 7.2.

The inventions are distinct, each from the other because:

Inventions Group I and Group II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the protein can be made by a materially different process such as via chemical synthesis, or it can be prepared from nature using various isolation/purification/chromatographic processes.

Furthermore, each of the products of Groups I and II, as well as the products of Groups III and IV encompass products (DNA, protein, antibody and mammals) that are structurally physically and functionally distinct, and if determined to be patentable they would also be patentably distinct. These groups are not required one for the other. For example the DNA can be used other than to make the protein or the mammal such as it's use as a probe or the use in other diagnostic processes. In a similar manner the protein, DNA or mammal do not require the antibody. Also the protein can be used other than to make the Ab or in the process of Group V, such as in therapy or it can be used diagnostically.

Inventions Group II and Group V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the

process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein, as claimed, can be used in a materially different processes, such as their use therapeutically, or they can be used as probes or in other diagnostic procedures. Further, these groups are not required one for the other.

The methods of Group I (process of making the protein), and of Group V (process of using the protein diagnostically) are distinct and not required one for the other because they use different elements/agents and steps, and the starting material and final outcomes of each are different.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classifications, as the searches are not co-extensive, and these are different issues for the search an examination of each which would be unduly burdensome. Accordingly, restriction for examination purposes as indicated is proper

During a telephone conversation with Stephen Malaska on 1-31-96 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-4 and 12-23. Affirmation of this election must be made by applicant in responding to this Office action. Claims 5-11 and 24-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143)

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the earlier filed application(s) in the first sentence of the specification (37 CFR 1.78).

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested for the elected invention: "DNA that encodes for A Novel Cytokine Designated LERK-6".

4. Claims 1,12,16,20, and 2,13,17,21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA that would encode for the full length/mature murine or human LERK-6 or specific fusion protein to such, does not reasonably provide enablement for any DNA that would encode for any protein or LERK-6 that binds hek/elk; or to any specie form of such. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 and its dependent claims which do not refer to those of 90% identity, are directed to any DNA that encodes for the protein by its name or its alphabetical designation as LERK-6 Referring to the encoded protein merely by its name does not serve to sufficiently define the claimed product, especially in the absence of the claim to recite a specific DNA sequence. The name of the encoded protein is arbitrarily assigned by the researcher who first isolate it and does not serve to sufficiently define the physical or functional characteristics of the protein. Further, while many researchers name or designate the protein because of a functional/biological protein that they observed, this is not sufficient as many protein, especially the cytokines, are pleiotropic in nature and possess some of the same or similar functional/biological properties as those associated with other distinct protein even to the point of the same or similar assay being used to detect a particular activity. Thus, to define the encoded protein merely by its name, which is generally associated with a function, is not sufficient to characterize a protein and to enable the skilled artisan to obtain such. Additionally, because of the multiple biological activities and functions that are associated with a protein, merely claiming it by its name creates further problems because it is well known that many protein have been referred to by different name (even though the names of the proteins may have been associated with different activities of the proteins), these names generally change to reflect a commonly designated and accepted name. But the physically make-up of the protein is the same despite the different names by which the

protein is referred. Because of the confusion created by such, the skilled artisan would encounter undue experimentation when trying to enable the protein by the limited characteristics of the claims. Exemplary of such is LERK-5 which is also known as HLK; as well as many other cytokines by the instant assignee. Furthermore, it has been shown that certain names of protein, when inadequately characterized, represent multiple forms of a protein, but once sufficiently characterized, these forms, although they initially were referred to by the same name or though to only represent one protein, become protein that are physically, functionally and patentably distinct. Exemplary of this is/was IL-1. In view of the various problems associated with this limited characterization, to define the encode protein by a name or abbreviation does not serve to sufficiently distinguish, define, identify or enable the encoded protein.

Claims 1,12,16 and 20 are further non-enabling for any DNA sequence that would encode the protein, nor is there enablement for any specie form of the encoded protein. In the absence of sufficient examples for the scope of the various DNA of the claims, the specification has not provided other evidence or guidance which would ensure these other forms to be predictive from the DNA for human or murine LERK-6 as recited in the Seq Identifiers. In the absence of a cellular source for these various forms and guidance that they are sufficiently identical to predict the DNA sequence of all other forms of the encoded protein, the skilled artisan would have to resort to undue experimentation to enable the full scope of the claims.

Claims 2,13,17 and 21 are directed to DNA sequences that are "at least 90% identical" On page 7, lines 7-14 of the specification state that nucleotide sequences that are at least 80-90% identical to the native LERK-6 sequence are contemplated by Applicant's invention. Since the native LERK-6 sequence consists of approximately 555 nucleotides, there would several different nucleotide sequences that could be postulated, given a constant 90% identical sequence to the native LERK-6 sequence with the last 100 nucleotides added on in every possible order. The numerous different nucleotide sequences do not take into account the added number of sequences that could be generated by dispersing the 100 nucleotide variations along the entire 555 base pair length of the entire sequence. Given the vast number of possible sequences that could be

encompassed given the constraints posed by the specification, there is no enablement or guidance provided in the specification as to what nucleotide insertions, deletions, or substitutions could be made to give 90% identity and still produce a functional extracellular domain, transmembrane region, cytoplasmic domain, or elk/hek binding regions (page 4, 6-8). Further in the absence of the specification setting forth regions that are critical for activity or for binding, and in the absence of structure/function studies providing sufficient examples of possible variations encompassed by the 90% identity, and further in the absence of sufficient guidance, it would constitute undue experimentation to enable the scope of these claims. Without guidance from the specification as to exactly what variance could occur in the nucleotide sequence, it would be undue experimentation for the skilled artisan to screen *all possible variants* to determine which had binding activity. Therefore, all possible variants of the LERK-6 nucleotide sequence that bind to elk and hek are neither described nor enabled, since the critical residues that confer this ability to the LERK-5 protein are at this time unknown.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions where the biological activity resides or regions directly involved in binding, stability, or catalysis; and in providing the correct three-dimensional spatial orientation for biologically active or binding sites, or for sites which represent other characteristics/properties of the protein. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990. Science, Vol.247, pp 1306-1310, especially p.1306, column 2, paragraph 2; and see Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz er (ed.), pages 433& 492-495; and Frommel et al/1985). However, Applicant has provided little or no guidance beyond the mere presentation of

sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions, insertions or deletions), and the nature and extent of changes that can be made in these positions in order to obtain protein that are 70%, 80% or 90% homologous. Such a definition might also read on previously characterized proteins, or alternatively, might include proteins with additional functions or activities neither envisioned nor enabled by applicants in the current invention. See Ex parte Forman, 230 U.S.P.Q. 546 (BPAI 1986) with regard to the issue raised above and In re Fisher, 166 USPQ 18.

Further, the cited portion of the specification does not even set forth art-recognized procedures for obtaining the various homologous proteins, and therefore is not adequate guidance for the vast number of mutants that are encompassed by the claims, but is rather a mere invitation to the artisan to use the current invention as a starting point for further experimentation. The scope of applicant's claims encompass modification on the protein that would be critical as well as non-critical for the biological activity of the protein. Thus, even if critical residues were identified, which in this case they are not, the mere identification of these critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the modified site must assume the proper three-dimensional configuration to be active-which conformation is dependent upon surrounding residues. The substitution/ insertion/deletion of non-essential residues can often destroy activity, therefore, it is deemed that to make each of the possible amino acid modifications for each of the non-essential residues, even if only conservative replacements were made, would also constitute undue experimentation. The introduction of non-conservative substitution, non-naturally occurring amino acids, deletions or insertions further raises the possible number of species. Therefore Applicant has not presented enablement commensurate in scope with the claims.

5. Claims 3-4,14-15,18-19,22-23 are free of the art.

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The citations to Shao et al and Cheng et al show 100% identity to the claimed

sequence, however, these citations are after applicants filing or benefit date. The other art is cited as of interest to show related art, or to support the 35 USC 112 scope rejection.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Garnette Draper whose telephone number is (703) 308-4232.

Draper/sg
March 7, 1997

GARNETTE D. DRAPER
PRIMARY EXAMINER
GROUP 1800